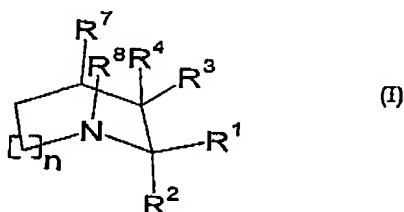




## ATTACHMENT B Amendments to the Claims

*This listing of claims will replace all prior versions, and listings, of claims in the application.*

1. (Original) Use of a compound capable of transferring wild type p53 from an inactive conformation thereof, which conformation is reactive to Pab 240 and not to Pab 1620, into an active conformation capable of inducing apoptosis, which compound is selected from compounds having a structure according to the formula I



wherein

n is 0, 1 or 2;

$R^1$  and  $R^2$  are the same or different and are selected from -H,  $-\text{CH}_2\text{-R}^5$ ,  $-\text{CH}_2\text{-O-R}^5$ ,  $-\text{CH}_2\text{-S-R}^5$ ,  $-\text{CH}_2\text{-NH-R}^5$ ,  $-\text{CO-O-R}^5$ ,  $-\text{CO-NH-R}^5$ ,  $-\text{CH}_2\text{-NH-CO-R}^5$ ,  $-\text{CH}_2\text{-O-CO-R}^5$ ,  $-\text{CH}_2\text{-NH-CO-NHR}^5$ ,  $-\text{CH}_2\text{-NH-CO-OR}^5$ ,  $-\text{CH}_2\text{-NH-CS-NHR}^5$  and  $-\text{CH}_2\text{-O-CO-NHR}^5$ ; or  $R^1$  and  $R^2$  are together  $=\text{CH}_2$ ;

$R^3$  and  $R^4$  are the same or different and are selected from -H, -OH, -SH,  $-\text{NH}_2$ , -NHR<sup>5</sup> and  $-\text{O-CO-C}_6\text{H}_5$ ; or  $R^3$  and  $R^4$  together are  $=\text{O}$ ,  $=\text{S}$ ,  $=\text{NH}$  or  $=\text{NR}^5$ ;

$R^5$  represents the same or different groups selected from H, substituted or non-substituted C1 to C10 alkyl, C2 to C10 alkenyl, C2 to C10 alkynyl, substituted or non-substituted C3 to C12 cycloalkyl, substituted or non-substituted benzyl groups, substituted or non-substituted aryl or mono-, bi-, tricyclic unsubstituted or substituted

heteroaromatic ring (s) with one or more heteroatoms and non-aromatic heterocycles wherein

the substituents of the substituted groups are selected from C1 to C10 alkyl, C2 to C10 alkenyl, C2 to C10 alkynyl, halogen, substituted or non-substituted aryl, substituted or non-substituted hetero-aromatic compounds, non-aromatic heterocycles, C1 to C10 alkyloxy, C1 to C10 alkylamino, C2 to C10 alkenylamino, C2 to C10 alkynylamino, COR<sup>6</sup>, CONR<sup>6</sup> and COOR<sup>6</sup>;

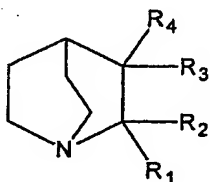
R<sup>6</sup> is selected from H, unsubstituted or substituted C1 to C10 alkyl, C2 to C10 alkenyl or alkynyl, benzyl, aryl, unsubstituted or substituted heteroaromatic rings with one or more hetero-atoms and non-aromatic heterocycles;

R<sup>7</sup> and R<sup>8</sup> together form a bridging CH<sub>2</sub>-CH<sub>2</sub> moiety; or R<sup>7</sup> and R<sup>8</sup> are both hydrogen;

or a pharmaceutically acceptable salt or prodrug thereof,

for the preparation of a medicament for use in treating malignant melanoma and/or a pathological condition involving undesired angiogenesis.

2. (Original) The use of claim 1, wherein the compound is selected from compounds having the following formula (II)



(II)

wherein:

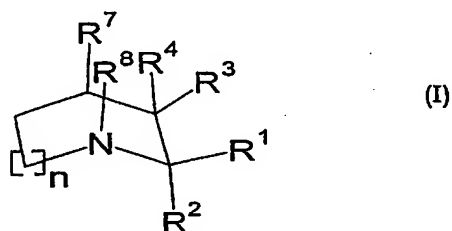
R<sub>1</sub> and R<sub>2</sub> are independently selected from hydrogen, hydroxymethyl, or a methylene group linked to the nitrogen atom of an amine-substituted phenyl group, to a nitrogen atom contained in the ring structure of a purine, 8-azapurine, or benzimidazol residue, or R<sub>1</sub> and R<sub>2</sub> may together represent a double bonded methylene group, and;

R<sub>3</sub> and R<sub>4</sub> are independently selected from hydrogen, hydroxyl, and benzoyloxy, or R<sub>3</sub> and R<sub>4</sub> may together represent an oxygen atom being double bonded, with the proviso that when either of R<sub>3</sub> and R<sub>4</sub> is a benzoyloxy group, both R<sub>1</sub> and R<sub>2</sub> are hydrogen, or a pharmaceutically acceptable salt or prodrug thereof.

3. (Original) The use of claim 2, wherein the compound is selected from 2,2bis(hydroxymethyl)-1-azabicyclo[2.2.2]octan-3-one, 9-(azabicyclo[2.2.2]octan-3-one)-6-chloro-9H-purine, 2-(hydroxymethyl)quinuclidine-3, 3-diol, 2-(adenine-9-methylene)-3-quinuclidinone, 2-methylene-3-quinuclidinone, 2-(2-amino-3-chloro-5-trifluoromethyl-1-methylaniline)-3-quinuclidinone, 2-(6-trifluoromethyl-4-chlorobenzimidazole-1-methylene)-3-quinuclidinone, 2-(6-methoxypurine-9-methylene)-3-quinuclidinone, 2-(8-azaadenine-9-methylene)-3-quinuclidinone, 1-azabicyclo[2.2.2]oct-3-yl benzoate, 2-(5,6-dimethyl-benzimidazole-1-methylene)-3-quinuclidinone, 2-(8-azaadenine-7-methylene)-3-quinuclidinone, 2-(7-methylene-1,3-dimethyluric acid)-3-quinuclidinone, or 2-(2,6-dichloro-9-methylenepurine)-3-quinuclidinone, or a pharmaceutically acceptable salt thereof.

4. (Currently Amended) The use of ~~anyone of the claims 1-3~~ together with a pharmaceutically acceptable carrier, diluent and/or excipient.

5. (Original) A method of treating malignant melanoma and/or inhibiting undesired angiogenesis, comprising administering to a mammal in need thereof a pharmaceutically efficient amount of a compound selected from compounds having a structure according to the formula I



wherein

n is 0, 1 or 2;

R<sup>1</sup> and R<sup>2</sup> are the same or different and are selected from -H, -CH<sub>2</sub>-R<sup>5</sup>, -CH<sub>2</sub>-O-R<sup>5</sup>, -CH<sub>2</sub>-S-R<sup>5</sup>, -CH<sub>2</sub>-NH-R<sup>5</sup>, -CO-O-R<sup>5</sup>, -CO-NH-R<sup>5</sup>, -CH<sub>2</sub>-NH-CO-R<sup>5</sup>, -CH<sub>2</sub>-O-CO-R<sup>5</sup>, -CH<sub>2</sub>-NH-CO-NHR<sup>5</sup>, -CH<sub>2</sub>-NH-CO-OR<sup>5</sup>, -CH<sub>2</sub>-NH-CS-NHR<sup>5</sup> and -CH<sub>2</sub>-O-CO-NHR<sup>5</sup>; or R<sup>1</sup> and R<sup>2</sup> are together=CH<sub>2</sub>;

R<sup>3</sup> and R<sup>4</sup> are the same or different and are selected from -H, -OH, -SH, -NH<sub>2</sub>, -NHR<sup>5</sup> and -O-CO-C<sub>6</sub>H<sub>5</sub>; or R<sup>3</sup> and R<sup>4</sup> together are =O, =S, =NH or =NR<sup>5</sup>;

R<sup>5</sup> represents the same or different groups selected from H, substituted or non-substituted C1 to C10 alkyl, C2 to C10 alkenyl, C2 to C10 alkynyl, substituted or non-substituted C3 to C12 cycloalkyl, substituted or non-substituted benzyl groups, substituted or non-substituted aryl or mono-, bi-, tricyclic unsubstituted or substituted

heteroaromatic ring (s) with one or more heteroatoms and non-aromatic heterocycles wherein the substituents of the substituted groups are selected from C1 to C10 alkyl, C2 to C10 alkenyl, C2 to C10 alkynyl, halogen, substituted or non-substituted aryl, substituted or non-substituted hetero-aromatic compounds, non-aromatic heterocycles, C1 to C10 alkyloxy, C1 to C10 alkylamino, C2 to C10 alkenylamino, C2 to C10 alkynylamino, COR<sup>6</sup>, CONR<sup>6</sup> and COOR<sup>6</sup>;

R<sup>6</sup> is selected from H, unsubstituted or substituted C1 to C10 alkyl, C2 to C10 alkenyl or alkynyl, benzyl, aryl, unsubstituted or substituted heteroaromatic rings with one or more hetero-atoms and non-aromatic heterocycles;

R<sup>7</sup> and R<sup>8</sup> together form a bridging CH<sub>2</sub>-CH<sub>2</sub> moiety; or R<sup>7</sup> and R<sup>8</sup> are both hydrogen;

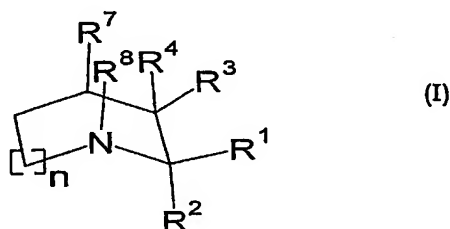
or a pharmaceutically acceptable salt or prodrug thereof.

6. (Original) Method of testing compounds for the ability of transferring wild type p53 from an inactive conformation into an active conformation comprising the steps:

- A. Providing cells carrying wt p53, in which cells inactive wt p53 conformation is present;
- B. Exposing the cells *in vitro* to a substance to be tested; and
- C. Measuring the cellular inactive wt p53 conformation.

7. (Original) The method of claim 6, wherein instead of step C an alternative step C' is used comprising comparing the effect of the tested substance on the cells (carrying functional p53) in step B to the effect on cells or tissues with no or non-functional p53.

8. (Currently Amended) The method of claim 6-~~or 7~~, wherein integrin  $\alpha_v\beta_3$  is present in the cells.
9. (Currently Amended) The method of claim 6-8, wherein the Pab 240 is used for detecting wt p53 in its inactive conformation.
10. (Currently Amended) The method of ~~any of the claims 6-9~~, wherein ~~a the~~ compound ~~of claim 1 is tested~~ is a compound is selected from compounds having a structure according to the formula I



wherein

n is 0, 1 or 2;

R<sup>1</sup> and R<sup>2</sup> are the same or different and are selected from -H, -CH<sub>2</sub>-R<sup>5</sup>, -CH<sub>2</sub>-O-

R<sup>5</sup>,

-CH<sub>2</sub>-S-R<sup>5</sup>, -CH<sub>2</sub>-NH-R<sup>5</sup>, -CO-O-R<sup>5</sup>, -CO-NH-R<sup>5</sup>, -CH<sub>2</sub>-NH-CO-R<sup>5</sup>,

-CH<sub>2</sub>-O-CO-R<sup>5</sup>, -CH<sub>2</sub>-NH-CO-NHR<sup>5</sup>, -CH<sub>2</sub>-NH-CO-OR<sup>5</sup>, -CH<sub>2</sub>-NH-CS-NHR<sup>5</sup> and

-CH<sub>2</sub>-O-CO-NHR<sup>5</sup>; or R<sup>1</sup> and R<sup>2</sup> are together =CH<sub>2</sub>;

R<sup>3</sup> and R<sup>4</sup> are the same or different and are selected from -H, -OH, -SH, -NH<sub>2</sub>, -

NHR<sup>5</sup> and -O-CO-C<sub>6</sub>H<sub>5</sub>; or R<sup>3</sup> and R<sup>4</sup> together are =O, =S, =NH or =NR<sup>5</sup>;

R<sup>5</sup> represents the same or different groups selected from H, substituted or non-substituted C1 to C10 alkyl, C2 to C10 alkenyl, C2 to C10 alkynyl, substituted or non-substituted C3 to C12 cycloalkyl, substituted or non-substituted benzyl groups, substituted or non-substituted aryl or mono-, bi-, tricyclic unsubstituted or substituted heteroaromatic ring (s) with one or more heteroatoms and non-aromatic heterocycles wherein the substituents of the substituted groups are selected from C1 to C10 alkyl, C2 to C10 alkenyl, C2 to C10 alkynyl, halogen, substituted or non-substituted aryl, substituted or non-substituted hetero-aromatic compounds, non-aromatic heterocycles, C1 to C10 alkyloxy, C1 to C10 alkylamino, C2 to C10 alkenylamino, C2 to C10 alkynylamino, COR<sup>6</sup>, CONR<sup>6</sup> and COOR<sup>6</sup>:

R<sup>6</sup> is selected from H, unsubstituted or substituted C1 to C10 alkyl, C2 to C10 alkenyl or alkynyl, benzyl, aryl, unsubstituted or substituted heteroaromatic rings with one or more hetero-atoms and non-aromatic heterocycles;

R<sup>7</sup> and R<sup>8</sup> together form a bridging CH<sub>2</sub>-CH<sub>2</sub> moiety; or R<sup>7</sup> and R<sup>8</sup> are both hydrogen;

or a pharmaceutically acceptable salt or prodrug thereof,

for the preparation of a medicament for use in treating malignant melanoma and/or a pathological condition involving undesired angiogenesis.

11. (Currently Amended) The method of ~~any of the claims 6-10~~, wherein the cells in step B are exposed *in vivo* in an animal to the substance to be tested, and the animal subsequently sacrificed.